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Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Roy A. Gravel et al.	Art Unit:	1623
Serial No.:	10/607,712	Examiner:	Not yet assigned
Filed:	June 27, 2003	Customer No.:	21559

Title: HUMAN METHIONINE SYNTHASE: CLONING, AND METHODS FOR EVALUATING RISK OF NEURAL TUBE DEFECTS, CARDIOVASCULAR DISEASE, AND CANCER

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Applicants submit the references listed on the attached form PTO 1449, copies of which are enclosed.

Under 35 U.S.C. § 120, this application relies on the earlier filing date of application serial number 08/980,326, which was filed on November 26, 1997. The following references were submitted to and/or cited by the Office in the prior application and, therefore, copies of these references are not provided for this application:

Bannerjee et al., GenBank Accession No. J04975, 1993.

Boushey et al., "A Quantitative Assessment of Plasma Homocysteine as a Risk Factor for Vascular Disease. Probable Benefits of Increasing Folic Acid Intakes," *JAMA* 274:1049-1057, 1995.

Chen et al., "Purification and Kinetic Mechanism of a Mammalian Methionine Synthase from Pig Liver," *J. Biol. Chem.* 269:27193-27197, 1994.

Chen, L.H. et al., "Human Methionine Synthase: Cdna Cloning, Gene Localization and Expression," *J. Biol. Chem.*, 272:3628-3634, 1997.

Drennan et al., "How a Protein Binds B12: A 3.0 A X-ray Structure of B12-binding Domains of Methionine Synthase," *Science* 266:1669-1674, 1994.

Fenton and Rosenberg, *The Metabolic and Molecular Bases of Inherited Disease*, McGraw-Hill, New York, pp. 3129-3149, 1995.

Fujii and Huennekens, "Activation of Methionine Synthetase by a Reduced Triphosphopyridine Nucleotide-dependent Flavoprotein System," *J. Biol. Chem.* 249:6745-6753, 1974.

Gulati et al., "Defects in Human Methionine Synthase in cblG Patients," *Hum. Molec. Genet.* 5:1859-1865, 1996.

LeClerc et al., GenBank Accession No. U71285, 1997.

Li et al., GenBank Accession No. U75743, 1997.

Li et al., "Cloning, Mapping and RNA Analysis of the Human Methionine Synthase Gene," *Hum. Molec. Genet.* 5:1851-1858, 1996.

Luschinsky et al., "Crystallization and Preliminary X-ray Diffraction Studies of the Cobalamin-binding Domain of Methionine Synthase from *Escherichia coli*," *J. Molec. Biol.* 225:557-560, 1992.

Marra et al., GenBank Accession No. W33307, 1996.

Mellman et al., "Genetic Control of Cobalamin Binding in Normal and Mutant Cells: Assignment of the Gene for 5-methyltetrahydrofolate: L-homocysteine S-methyltransferase to Human Chromosome 1," *Proc. Natl. Acad. Sci. USA* 76:405-409, 1979.

Mills et al., "Homocysteine Metabolism in Pregnancies Complicated by Neural-Tube Defects," *Lancet* 345:149-151, 1995.

Rosenblatt et al., *The Metabolic and Molecular Basis of Inherited Disease*, McGraw-Hill, New York, pp. 3111-3128, 1995.

Rosenblatt et al., "Altered Vitamin B_{12} Metabolism in Fibroblasts from a Patient with Megaloblastic Anemia and Homocystinuria Due to a New Defect in Methionine Biosynthesis," *J. Clin. Invest.* 74:2149-2156, 1984.

Rozen et al., "Molecular Genetic Aspects of Hyperhomocysteinemia and its Relation to Folic Acid," *Clin. Invest. Med.* 19:171-178, 1996.

Schuh et al., "Homocystinuria and Megaloblastic Anemia Responsive to Vitamin B12 Therapy. An Inborn Error of Metabolism due to a Defect in Cobalamin Metabolism," *N. Engl. J. Med.* 310:686-690, 1984.

Sillaots et al. "Heterogeneity in cblG: Differential Retention of Cobalamin on Methionine Synthase," *Biochem. Med. Metab. Biol.* 47:242-249, 1992.

Steegers-Theunissen et al., "Maternal Hyperhomocysteinemia: A Risk Factor for Neural-tube Defects?" *Metab. Clin. Exp.* 43:1475-1480, 1994.

Watkins et al., "Genetic Heterogeneity Among Patients with Methylcobalamin Deficiency. Definition of Two Complementation Groups, cblE and cblG," *J. Clin. Invest.* 81:1690-1694, 1988.

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Submission of this statement is not a representation that a search has been made nor is information included in this statement an admission that the information is material to patentability.

This statement is being filed before the receipt of a first Office action on the merits. Please apply any charges or credits to Deposit Account 03-2095.

Respectfully submitted,

Date: June 3, 2004

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SUBSTITUTE FORM PTO-1449 (MODIFIED) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	Attorney Docket No.	50004/002005
	Serial No.	10/607,712
	Applicants	Roy A. Gravel et al.
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)	Filing Date	June 27, 2003
	Group	1623
	IDS Filed	June 3, 2004
(37 C.F.R. § 1.98(b))	Customer No.	21559

U.S. PATENTS

Examiner's Initials	Patent Number	Issue Date	Patentee	Class	Subclass	Filing Date (If Appropriate)
	6,677,436	01/13/04	Sato et al.			

FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION

Examiner's Initials	Document Number	Publication Date	Country or Patent Office	Class	Subclass	Translation (Yes/No)

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)

	Bannerjee et al., GenBank Accession No. J04975, 1993.
	Boushey et al., "A Quantitative Assessment of Plasma Homocysteine as a Risk Factor for Vascular Disease. Probable Benefits of Increasing Folic Acid Intakes," *JAMA* 274:1049-1057, 1995.
	Brasch et al., "Neonatal Megaloblastic Anemia Associated with Reduced Cellular Uptake of Folate and Low Methyl-B12 Levels: A New Mutation," *Aust. N. Z. J. Med.* 18 Supp. 434, 1988.
	Chen et al., "Purification and Kinetic Mechanism of a Mammalian Methionine Synthase from Pig Liver," *J. Biol. Chem.* 269:27193-27197, 1994.
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	Fenton and Rosenberg, *The Metabolic and Molecular Bases of Inherited Disease*, McGraw-Hill, New York, pp. 3129-3149, 1995.
	Frosst et al., "A Candidate Genetic Risk Factor for Vascular Disease: A Common Mutation in Methylenetetrahydrofolate Reductase," *Nat. Genet.* 10:111-113, 1995.
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	Goyette et al., "Human Methylenetetrahydrofolate Reductase: Isolation of cDNA, Mapping and Mutation Identification," *Nat. Genetics* 7:195-200, 1994.
	Gulati et al., "Defects in Human Methionine Synthase in cblG Patients," *Hum. Molec. Genet.*, 5:1859-1865, 1996.
	Leclerc et al., "Molecular Cloning, Expression and Physical Mapping of the Human Methionine Synthase Reductase Gene," *Gene* 240:75-88, 1999.

EXAMINER	DATE CONSIDERED

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.

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	Li et al., "Cloning, Mapping and RNA Analysis of the Human Methionine Synthase Gene," *Hum. Molec. Genet.* 5:1851-1858, 1996.
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	Wilson et al., "A Common Variant in Methionine Synthase Reductase Combined with Low Cobalamin (Vitamin B_{12}) Increase Risk for Spina Bifida," *Molec. Genet. Metab.* 67:317-323, 1999.
	Wilson et al., "Molecular Basis for Methionine Synthase Reductase Deficiency in Patients Belonging to the cblE Complementation Group of Disorders in Folate/Cobalamin Metabolism," *Hum. Molec. Genet. 8*:2009-2016, 1999.

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